

WHAT IS CLAIMED IS:

1. A human keratinocyte growth factor (KGF) having an apparent molecular weight of about 28 kDa as determined by migration in NaDodSO₄/PAGE, and a specific activity of at least about 3.4×10^4 units per milligram of protein, where one unit of activity is defined as that amount which causes half of the maximal possible stimulation of DNA synthesis in BALB/MK keratinocyte cells under standard assay conditions.

2. Human KGF according to claim 1, wherein said specific activity is at least about 3.2×10^5 units per milligram protein.

3. A bioassay for KGF-like activity in a test sample which comprises the following steps:

i) growing keratinocytes in culture to confluence and maintaining said confluent culture in serum-free medium;

ii) adding a test sample to said confluent culture of keratinocytes;

and

iii) determining the stimulation of DNA synthesis in said keratinocytes.

4. A method of producing KGF from cultured cells comprising the following steps:

- i) Culturing KGF-producing cells in culture medium under conditions such that KGF is produced;
- ii) concentrating said culture medium so that a first concentrate is formed;
- iii) contacting said concentrate with heparin under conditions such that KGF present in said first concentrate binds to the heparin whereby a heparin-KGF complex is formed;
- iv) separating said heparin-KGF complex from said concentrate;
- v) treating said heparin-KGF complex under conditions such that said KGF dissociates from the heparin so that a solution of free KGF is formed;
- vi) concentrating said solution so that a second concentrate is formed;
- vii) fractionating said second concentrate so that KGF is separated from the remaining components.

5. A method of producing KGF from cultured cells, according to claim 4, wherein said KGF-producing cells are M426 human embryonic fibroblasts.

5 6. A DNA segment encoding a human keratinocyte growth factor (KGF) protein.

7. A DNA segment, according to claim 6, wherein said protein has the amino acid sequence defined in Figure II-1.

10 8. A DNA segment encoding a chimeric KGF-like protein which comprises within a single polypeptide molecule functional segments of human KGF and at least one other polypeptide of the fibroblast growth factor family.

15 9. A recombinant DNA molecule comprising a DNA segment according to claim 6 or claim 8 and a vector.

20 10. A culture of cells transformed with said recombinant DNA molecule according to claim 9.

25 11. A method of producing a human KGF protein comprising culturing said cells according to claim 10 in a culture medium under conditions such that said protein is produced and isolating said protein from said cells.

12. A method of producing a human KGF protein comprising culturing said cells according to claim 10 in a culture medium, wherein said

protein is secreted from said cell, and isolating said protein from said medium.

13. A human KGF or KGF-like protein having the amino acid sequence in Figure II-1B.

5 14. A human KGF or KGF-like protein, according to claim 13, which is not glycosylated.

15. An antibody specific for a peptide having the amino acid sequence of human KGF or KGF-like protein, according to claim 13.

10 16. The antibody according to claim 15 which neutralizes the mitogenic activity of human KGF.

17. A bioassay for expression of a gene encoding KGF, comprising the steps of:

15 i) isolating mRNA from tissues or cells;

and

ii) annealing said RNA to a DNA probe encoding a human KGF;

20 iii) determining the amount of DNA:RNA hybrid containing said DNA probe.

18. A bioassay for KGF antigen
comprising the steps of:

i) extracting polypeptides from body
fluids or tissue samples;

5 and

ii) determining the level of human KGF
antigen by reaction with an
antibody specific for a peptide
having the amino acid sequence of
10 human KGF or KGF like protein,
according to claim 13.

19. A pharmaceutical composition for
treatment of conditions requiring specific
stimulation of epithelial cells, comprising KGF
15 according to claim 1 or claim 13, and an
acceptable pharmaceutical carrier.

20. A pharmaceutical composition for
treatment of conditions requiring specific
inhibition of stimulation of epithelial cells by
20 KGF, comprising antibodies to KGF according to
claim 15, and an acceptable pharmaceutical
carrier.

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